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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,942	12/05/2001	Robert J. Hariri	9516-100-999	7788

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,942	HARIRI, ROBERT J.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 25, 29-36, 40-46, 49-55, 60- 66, 68, 70-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 25, 29-36, 40-46, 49-55, 60- 66, 68, 70-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9/28/04* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response filed 9/28/04 have been entered. Claims 26, 27, 37-39, 47, 48, 56-59, 67 and 69 have been canceled. Claims 29-31, 49-51 have been amended. Claims 70-77 are newly submitted. It is noted that Claims 70-72 are newly submitted claims but wrongly identified as "currently amended". Claims 1, 25, 29-36, 40-46, 49-55, 60- 66, 68, 70-77 pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-31 are newly rejected under 35 U.S.C. 112 first paragraph, because the specification as originally filed does not describe the invention as now claimed. The original disclosure fails to teach "culturing" the placenta before perfusing as now claimed. The subject matter is now considered to be new matter.

MPEP 2163.06 notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS

INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added). MPEP 2163.02 teaches that "WHENEVER THE ISSUE ARISES, THE FUNDAMENTAL FACTUAL INQUIRY IS WHETHER A CLAIM DEFINES AN INVENTION THAT IS CLEARLY CONVEYED TO THOSE SKILLED IN THE ART AT THE TIME THE APPLICATION WAS FILED...IF A CLAIM IS AMENDED TO INCLUDE SUBJECT MATTER, LIMITATIONS, OR TERMINOLOGY NOT PRESENT IN THE APPLICATION AS FILED, INVOLVING A DEPARTURE FROM, ADDITION TO, OR DELETION FROM THE DISCLOSURE OF THE APPLICATION AS FILED, THE EXAMINER SHOULD CONCLUDE THAT THE CLAIMED SUBJECT MATTER IS NOT DESCRIBED IN THAT APPLICATION". The amended claims 29-31 require "said placenta is *cultured* for at least four hours after removal of said residual blood and prior to said perfusing", applicants pointed to page 5, last paragraph of the specification as support for the amendment. However, it is noted that the cited paragraph describes a process of draining and storing a placenta, and did not mention "culture" the placenta. The cited paragraph teaches that the placenta is placed in a sterile basin, washed with 500 ml of buffered saline, and maintained for a period of 2-24 hours. This process differs from culturing process because tissue culture is a process of growing tissue in a prepared nutrient medium (see e.g. Merriam-Webster's Online Dictionary 2004), which involve further cell growth and proliferation. Moreover, the specification teaches "the placenta is maintained...for a period varying from 2-24 hours", yet the amended claim 31 recites "placenta is cultured for at least 24 hours", which encompasses a period longer than 24 hrs. Thus, the amendment is a departure from or an

addition to the disclosure of the application as filed, accordingly, it introduces new matter into the disclosure.

For reasons set forth above, the amendment filed 9/28/04 is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. Applicant is required to cancel the new matter in the reply to this Office Action.

To the extent that the claimed methods are not described in the instant disclosure, claims 29-31 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Claims 1, 25, 29-36, 40-46, 49-55, 60- 66, 68, stand rejected, and claims 70-77 are newly under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for reasons of record and following.

In the response, applicants first argue that the Examiner does not explain how the disclosure fails to enable the full scope of the claims, and what would ostensibly be required to practice the claimed invention. What experimentation is undue.

In response, the claimed invention being collecting stem cells, the specification fails to teach whether the collected cells are indeed stem cells. This opinion is reflected and explained in the following passage (page 4 of the Office action mailed 6/15/04):

These claims are drawn to a novel method of obtaining residual stem cells within the parenchyma and extra-vascular space of a placenta. However, the specification only describes that there are morphologically very different cell types within the isolated cell population and contemplates isolating cells with markers such as CD34 and CD38 (Specification, paragraph bridging pages 11-12, and fig. 4). However, the specification fails to disclose any data that illustrates the functional characteristics of isolated cells, e.g. what kind of surface markers they bear, whether they are terminally differentiated, monopontent progenitor cells, or multipotent or totipotent stem cells. Although it is known in the art that the cord blood cells comprise multipotent cells, it is unknown and the specification fails to disclose that residual cells from the extra-vascular space of a placenta contain multipotent stem cells, and they differ from cells collected from the extra-vascular space of any connective tissue. Accordingly, the specification fails to provide an enabling disclosure for what is now claimed.

The scope perceived by the Examiner is the enablement of collecting stem cells vs. collecting any cells from the perfused placenta. When claims is aimed at collecting stem cells, the disclosure should teach that the stem cells are indeed collected.

Applicants then argue that the specification teaches in page 12 that at least one population of cells had characteristics very similar to bone marrow-derived mesenchymal stem cells.

In response, "very similar" is not sufficient teaching to enable the claimed invention. Particularly considering such similarity is drawn based on comparisons under a phase microscopy of the rounded cells (Specification, page 12, lines 3-6). Although the phase-contrast microscope is an excellent aid for observing

living cells, it is not a common tool for histological confirmation of the identity of a cell. In cell biology, to be certain of any type of cells, particularly stem cells, the skilled in the art needs to identify the proliferation and differentiation ability of the cells, surface markers of the cells as well as the histology of the stained cells under stereoscopic microscope and electron microscope. These are evidenced in the teaching of *van Bekkum*, for example, tables 1-4 and figure 1 (IDS/C10). Further, claim 25 and dependent claims are drawn to collecting CD34+ stem cells, however, the specification fails to teach that such CD34+ stem cells are indeed isolated from the perfused placenta, which is free of residual cord blood. Accordingly, the specification fails to provide an enabling disclosure for what is now claimed. It would have required undue experimentation for the skilled in the art intending to practice the invention to find out for themselves whether the cells isolated from said placenta are indeed stem cells. To this end, the court states, "LAW REQUIRES THAT THE DISCLOSURE IN APPLICATION SHALL INFORM THOSE SKILLED IN THE ART HOW TO USE APPLICANT'S ALLEGED DISCOVERY, NOT HOW TO FIND OUT HOW TO USE IT FOR THEMSELVES" *In re Gardner* 166 USPQ 138 (CCPA) 1970

Applicants then argue the assertion of none enablement does not take into account that placental perfusion is a well-developed art, and pointed to the cited art in the previous Office action and the newly submitted dissertation of *Myllynen*.

In response, the lack of enablement is not due to the process of placenta perfusion but the identity of the cells collected. In the cited references of record, the skilled artisans collect cord blood stem cells from a placenta or collect secretive substances from existing placenta cells. The references are not drawn

to collecting stem cells after the removal of residue cord blood as instantly claimed. Thus, the cited art could not support the enablement of instantly claimed invention.

Applicants then argue that the specific characteristics of the stem cells collected is irrelevant as long as the stem cells are necessarily obtained when one follows the claimed method. Applicants also argue the characteristics of various stem cells are well known in the art such as taught by van Bekkum, 1990, and Caplan 1994.

The argument is not persuasive because the specification fails to teach or disclose that the stem cells are necessarily present. With respect to the cited references, *van Bekkum* describes the stem cells in the bone marrow, not any part of the placenta or within the parenchyma and extra-vascular space of a placenta. *Caplan* describes the mesengenic process, again, does not teach that the MSCs are necessarily present within the parenchyma and extra-vascular space of a placenta. Accordingly, neither the specification nor the cited art support the enablement of instantly claimed invention.

Applicants go on to argue that the Examiner states, "These claims are drawn to a novel method of obtaining residual stem cells within the parenchyma and extra-vascular space of a placenta" and "the specification fails to disclose that the residual cells from the extra-vascular space of a placenta contain multipotent stem cells", but the claims do not recite the term "extravascular space or requires that the recited stem cells originate in a particular part of the placenta.

Applicants thus allege that the Examiner reading a limitation into the claim, and faulting the specification for not including that limitation.

In response, the statement of the Examiner was drawn from reading the limitation of the claims in light of the teaching of the specification. This is a proper method of patent examination. For example, claim 1 recites, "perfusing said placenta... for a time sufficient to collect a detectable amount of stem cells from said placenta, said placenta having been drained of cord blood and flushed to remove residual blood prior to said perfusing". Any person with a common sense and basic medical knowledge would consider if there is no residual blood, where the stem cells come from during the placenta perfusion. This question is addressed by the specification. Under "Summary of the Invention", the specification teaches, "The placenta is then processed in such a manner as to establish an ex vivo, natural bioreactor environment in which resident stem cells within the parenchyma and extravascular space are recruited and migrate into the empty microcirculation, where they can be washed into a collecting vessel by perfusion" (Specification, page 3). Apparently, it is the specification that teaches where the stem cells come from.

Applicants then argue that it does not matter which parts of the placenta the stem cells come from, and applicants are not required to explain why, only to teach how to make and use it, and the method steps are straightforward as claimed.

In response, the Office does not require the applicants to know exactly which part of the placenta the stem cells are from, but require the applicants to

provide evidence that the isolated cells from perfusion solution are indeed stem cells, and CD34+ stem cells. Since the preamble of the claims states a method of isolating stem cells from a perfused placenta, it is proper to evaluate the enablement of the preamble, and it is essential for applicants to provide sufficient guidance to prove that the stem cells are indeed in the collected perfusing solution, and such should be easy to prove if there are indeed stem cells.

The following is a further explanation regarding "how to make" and "how to use" standard in M.P.E.P. According to MPEP as pursuant to an enabling disclosure required by 35 U.S.C 112, first paragraph,

"AN APPLICANT'S SPECIFICATION MUST ENABLE A PERSON SKILLED IN THE ART TO MAKE AND USE THE CLAIMED INVENTION WITHOUT UNDUE EXPERIMENTATION.(...) AS SUCH, THE DISCLOSURE MUST TEACH A PERSON SKILLED IN EACH ART HOW TO MAKE AND USE THE RELEVANT ASPECT OF THE INVENTION WITHOUT *UNDUE* EXPERIMENTATION. FOR EXAMPLE, TO ENABLE A CLAIM TO A PROGRAMMED COMPUTER THAT DETERMINES AND DISPLAYS THE THREE-DIMENSIONAL STRUCTURE OF A CHEMICAL COMPOUND, THE DISCLOSURE MUST

- ENABLE A PERSON SKILLED IN THE ART OF MOLECULAR MODELING TO UNDERSTAND AND PRACTICE THE UNDERLYING MOLECULAR MODELING PROCESSES; AND
- ENABLE A PERSON SKILLED IN THE ART OF COMPUTER PROGRAMMING TO CREATE A PROGRAM THAT DIRECTS A COMPUTER TO CREATE AND DISPLAY THE IMAGE REPRESENTING THE THREE-DIMENSIONAL STRUCTURE OF THE COMPOUND.

IN OTHER WORDS, THE DISCLOSURE CORRESPONDING TO EACH ASPECT OF THE INVENTION MUST BE ENABLING TO A PERSON SKILLED IN EACH RESPECTIVE ART. (MPEP 2106.B.2)

Thus, according to this standard, the stem cells collected by the method must be disclosed as necessarily present. The specification fails to disclose this aspect of the invention, thus fails to meet the statutory enablement requirement.

Accordingly, for reasons of record and those set forth *supra*, it is maintained that the specification fails to provide an enabling disclosure for the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-51 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amended claims 49-51 are vague and indefinite because of the claim recitation, "said perfusing is performed at least x hours after removal of said residual blood". The phase could be interpreted either as "the perfusion will not begin until x hours have passed after removal of said residual blood", or "the perfusion is performed for a period of x hours after removal of said residual blood", for example. It is unclear what applicants intend to claim, and thus the metes and bounds of the claims are uncertain.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory

period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Q. Janice Li
Primary Examiner
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QL
December 9, 2004